Effectiveness of gestational diabetes treatment: a systematic review with quality of evidence assessment

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CRD summary
This review concluded that gestational diabetes treatment compared to usual antenatal care effectively reduced large for gestational age at birth, macrosomia, shoulder dystocia, pre-eclampsia and hypertensive disorders without compromising safety. The authors' conclusions reflect the evidence but the evidence base was small for some outcomes and the potential risk of bias in the included studies limits the reliability of the findings.

Authors' objectives
To assess the effectiveness of gestational diabetes treatment compared to usual antenatal care in the prevention of adverse pregnancy outcomes.

Searching
Fourteen electronic databases (including EMBASE, PubMed and ClinicalTrials.gov) were searched from inception to February 2012 without language restrictions. Search terms were reported. Reference lists of review articles and relevant studies were screened manually.

Study selection
Eligible studies were randomised or quasi-randomised controlled clinical trials that compared gestational diabetes treatment to usual antenatal care in the prevention of adverse pregnancy outcomes in women with gestational diabetes. Perinatal and maternal outcomes were as defined in the review.

Included trials were conducted in USA, UK, Canada, Australia and Hong Kong between 1974 and 2009. Mean ages of participants ranged from 28.3 to 30.8 years. Diagnostic criteria for gestational diabetes varied slightly between trials. All interventions included a dietary element and some also including glucose monitoring. In most trials between 8% and 100% of the women received insulin treatment.

Two reviewers independently screened studies for inclusion. Discrepancies were resolved through discussion.

Assessment of study quality
Two reviewers assessed risk of bias based on Cochrane methods and rated each trial as being at high, uncertain or low risk of bias. Discrepancies between reviewers were resolved through discussion. The level of evidence was assessed for each outcome.

Data extraction
Two reviewers independently extracted quantitative data; where this was not available, approximate values were estimated from figures or calculated from proportions. Any discrepancies between reviewers were resolved through discussion.

Methods of synthesis
A fixed-effect model (or random-effects model where there was evidence of statistical heterogeneity) was used to combine data to calculate relative risks and 95% confidence intervals. The number needed to treat (NNT) was estimated.

Statistical heterogeneity was assessed using the $\chi^2$ test and $I^2$ statistic ($I^2>50\%$ indicated high heterogeneity). Sensitivity analysis was performed based on trial allocation concealment and type of random-effects model used (restricted maximum-likelihood variance estimator, maximum likelihood, empirical Bayes, Sidik-Jonkman and DerSimonian and Laird).

Trial sequential analysis was performed for various outcomes (as reported in the review) to determine whether the
available evidence was sufficient.

Funnel plots, Egger’s test and trim-and-fill methods were used to assess publication bias when at least five studies reported an outcome.

**Results of the review**

Seven trials (3,157 women) were included in the review. Four trials used random allocation and three used quasi-randomisation. Allocation concealment methods were reported in two trials. None of the trials were double blind. One trial had incomplete outcome data.

**Perinatal outcomes**

High quality evidence suggested that women treated for gestational diabetes were at significantly lower risk for infants large for gestational age at birth (RR 0.57, 95% CI 0.47 to 0.71; NNT=12; four trials; I²=0%) and macrosomia (RR 0.47, 95% CI 0.34 to 0.65; NNT=11; six trials; I²=48.2%) compared to women who received usual antenatal care. Favourable findings for the intervention were reported for shoulder dystocia (RR 0.41, 95% CI 0.22 to 0.76; NNT=49; two trials; I²=0%) but the level of evidence was low. There were no differences between treatment groups for the remaining outcomes.

**Maternal outcomes**

Moderate quality evidence showed that treatment for gestational diabetes significantly reduced the risk of pre-eclampsia (RR 0.61, 95% CI 0.46 to 0.81; NNT=21; two trials; I²=0%) and hypertensive disorder (RR 0.64, 95% CI 0.51 to 0.81; NNT=18; three trials; I²=0%) compared to usual antenatal care. There were no significant differences between treatment groups for caesarean section or diabetes later in life.

Sensitivity analyses did not significantly alter the findings. Sequential analyses suggested that trials had sufficient data to make inferences for macrosomia, large for gestational age at birth, hypertensive disorders and caesarean section.

There was little evidence of publication bias according to funnel plots which suggested only a small impact on the strength of the association.

**Authors’ conclusions**

Treatment of gestational diabetes mellitus is effective in reducing large for gestational age at birth, macrosomia, shoulder dystocia, pre-eclampsia and hypertensive disorders during pregnancy, without compromising safety. However, the evidence cannot determine the extent to which these benefits accrue from other interventions.

**CRD commentary**

A comprehensive literature search was undertaken without language or publication status restrictions. Formal assessment for publication bias suggested a small potential risk for bias. Trial quality was assessed and was considered adequate by the authors. However, all trials were at risk of some bias and none of the trials were double blinded. Each stage of the review process was performed in duplicate, which reduced potential for reviewer error and bias.

Thorough analyses were undertaken but it was unclear whether appropriate methods were used to estimate approximate outcome values from figures or proportions. Trial sample sizes lacked power for some outcomes and this was highlighted by the authors.

The authors acknowledged the 40-year time span across the trials during which time treatment methods will have changed considerably. They also acknowledged differences across trials in diagnosis of gestational diabetes and use of insulin.

The authors’ conclusions reflect the evidence but the limited number of studies, small sample sizes for some outcomes and the potential risk of bias in studies limits the reliability of the findings.

**Implications of the review for practice and research**

**Practice**: The authors stated that their findings justified treatment of gestational diabetes but implications for specific diagnostic criteria were limited. The authors stated that the generalisability of the findings on the benefits of treating milder cases of gestational diabetes and for low income countries was unclear.

**Research**: The authors did not state any implications for research.
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